

**REMARKS:**

By the present amendment, claims 19, 23 and 27 have been amended to replace the expression "inhibitor of CYP2A6" with "inhibitor of CYP2B6" to correct an obvious typographical error and restore the claims to their previous form. Claims 19, 23 and 27 have also been amended to remove the term "nitrosodialkylamines". Further, claims 19, 23 and 27 have been amended to remove the terms miconazole, clotrimazole and pilocarpine since they are specific examples of imidazole antimycotics which are already present in the list of substances in these claims. Miconazole, clotrimazole and pilocarpine have been reinserted in new claims 47-49.

Claims 20, 24 and 28 have been cancelled.

Claim 27 has been amended to remove the comma between "imidazole" and "antimycotic" to correct an obvious typographical error.

The amendments made to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants submit that no new matter has been added to the claims as a result of these amendments. Entry of the claim amendments is respectfully requested.

The Official Action dated September 11, 2006 has been carefully considered. It is believed that the amended claims submitted herewith and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

**35 USC §112, First Paragraph**

The Examiner has objected to claim 27 under 35 USC §112, First Paragraph, as failing to comply with the Written Description requirement. The Examiner objected to the word antimycotic in the list of CYP2A6 inhibitors. Claim 27 has been amended to remove the comma between the words "antimycotic" and "imidazole" as suggested by the Examiner to obviate this objection.

In light of the above amendment, the Applicants request that the Examiner's objection to claim 27 under 35 USC §112, First Paragraph, be withdrawn.

### **35 USC §112, Second Paragraph**

The Examiner has objected to claims 19, 23 and 27 under 35 USC §112, Second Paragraph as it is unclear what the difference would be in an agent that selectively inhibits CYP2A6 and an inhibitor of CYP2A6. Claims 19, 23 and 27 have been amended to replace the expression "inhibitor of CYP2A6" with "inhibitor of CYP2B6" to restore these claims to their previous form and to correct a typographical error. The Applicants submit that claims 19, 23 and 27 are now in compliance with 35 USC §112, Second Paragraph.

In light of the above amendment, the Applicants request that the Examiner's objection to claims 19, 23 and 27 under 35 USC §112, Second Paragraph, be withdrawn.

The Examiner has objected to the term "enhancing" in claim 19 under 35 USC §112, Second Paragraph, alleging that it is a relative term that renders the claim indefinite. The Applicants respectfully disagree with the Examiner. A person skilled in the art would readily understand that the term "enhance" means any increase over a baseline amount, which in this case is the inhibition of nicotine metabolism by a CYP2A6 inhibitor in the absence of the substance and the CYP2B6 inhibitor. Accordingly, the Applicants submit that a person skilled in the art would understand that any administration of an effective amount of substance which inhibits CYP2A6 and an effective amount of a CYP2B6 inhibitor that enhances inhibition of nicotine metabolism by a CYP2A6 inhibitor to any degree compared to otherwise similar conditions, except for in the absence of said administration, would infringe claim 19.

In light of the above, the Applicants request that the Examiner's objection to claim 19 under 35 USC §112, Second Paragraph, be withdrawn.

The Examiner has objected to claims 19 and 23 under 35 USC §112, Second Paragraph, as it recites the broad genus of imidazole antimycotics along with the narrow species, miconazole, which is a specific example of an imidazole antimycotic. Claims 19 and 23 have been amended to remove the species, miconazole, clotrimazole and pilocarpine, since they are all specific examples of imidazole antimycotics. These species have been reinserted as new dependent claims.

In light of the above amendment, the Applicants request that the Examiner's objection to claims 19 and 23 under 35 USC §112, Second Paragraph, be withdrawn.

### **35 USC §102(b)**

The Examiner has objected to claim 23 under 35 USC §102(b) as being anticipated by Vinals et al. (U.S. Patent No. 3,977,418). The Examiner alleges that Vinals teaches a composition comprising nicotine and coumarin (a substance that inhibits CYP2A6). Claim 23 has been amended to restore it to its previous form, i.e. so that it is directed to a pharmaceutical composition for regulating the metabolism of nicotine to cotinine comprising an effective amount of a substance which selectively inhibits CYP2A6 and an effective amount of an inhibitor of CYP2B6. Since Vinals et al. does not teach compositions comprising a substance which selectively inhibits CYP2A6 and an inhibitor of CYP2B6, this reference does not anticipate claim 23. This amendment in no way means that the Applicants agree with the Examiner's objection. The claims have merely been amended to correct a typographical error, said correction obviating the Examiner's objection.

In light of the above amendment, the Applicants request that the Examiner's objection to claim 23 under 35 USC §102(b) be withdrawn.

The Examiner has objected to claim 24 under 35 USC §102(b) as being anticipated by Choudhury et al. Cancer Letters (1995). Claim 24 has been cancelled by

the present amendment, therefore the Examiner's objection to this claim has been rendered moot.

In light of the above amendment, the Applicants request that the Examiner's objection to claim 24 under 35 USC §102(b) be withdrawn.

### **35 USC §103(a)**

The Examiner has objected to claims 19, 20, 27, 28 and 39-41 under 35 USC §103(a) as being obvious in light of Berkman et al. Biochemical Pharmacology (1995) in view of Seaton et al. Pharmac. Ther. 1993 and Draper et al. Arch. Biochem. Biophys (1997). The Examiner alleges that teachings in the cited references make it obvious to one of ordinary skill in the art to inhibit the CYP2A6 enzyme to inhibit metabolism of nicotine. Claims 19, 23 and 27, and accordingly claims 39-41 dependent thereon, have been amended to restore them to their previous form, i.e. so that they are directed to a methods and composition for regulating the metabolism of nicotine to cotinine involving the use of an effective amount of a substance which selectively inhibits CYP2A6 and an effective amount of an inhibitor of CYP2B6. Since none of the cited art teaches or remotely suggests the combination of a CYP2A6 and CYP2B6 inhibitor, claims 19, 23 and 27, and 39-41 are in compliance with 35 USC §103(a). This amendment in no way means that the Applicants agree with the Examiner's objections. The claims have merely been amended to correct a typographical error, said correction obviating the Examiner's objection. Claims 20 and 28 have been cancelled by the present amendment, rendering the Examiner's objection to these claims moot.

In light of the above amendment, the Applicants request that the Examiner's objection to claims 19, 20, 27, 28 and 39-41 under 35 USC §103(a) be withdrawn.

In view of the foregoing comments and amendments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the foregoing response in

greater detail, the Examiner is invited to contact Patricia Folkins by telephone at (416) 957-1683 at the Examiner's convenience.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'P. Folkins', is written over a horizontal line.

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